Isis Pharmaceuticals, Inc.

Colleen J. McKieman, PhD

March 10, 2005

Signature
Printed name

Date

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PTO/SB/21 (09-04) Approved for use through 07/31/2006. OMB 0651-0031 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid CMB control number. Application Number 10/530 399 TRANSMITTAL Filing Date July 30, 2003 First Named Inventor FORM C. Frank Bennett Art Unit 1635 Examiner Name Amy Hudson Bowman (to be used for all correspondence after initial filing) Attorney Docket Number RTS-0324US.C1 Total Number of Pages in This Submission **ENCLOSURES** (Check all that apply) After Allowance Communication to TC Fee Transmittal Form Drawing(s) Appeal Communication to Board Licensing-related Papers Fee Attached of Appeals and Interferences Appeal Communication to TC 1 Amendment/Reply (Appeal Notice, Brief, Reply Brief) Petition to Convert to a Proprietary Information After Final Provisional Application Power of Attorney, Revocation Affidavite/declaration(s) Status Letter Change of Correspondence Address Other Enclosure(s) (please Identify Terminal Disclaimer Extension of Time Request below): Request for Refund Express Abandonment Request CD, Number of CD(s) Information Disclosure Statement Landscape Table on CD Certified Copy of Priority Remarks Document(s) Reply to Missing Parts/ Incomplete Application Reply to Missing Parts under 37 CFR 1.52 or 1.53 SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT Firm Name

CERTIFICATE OF TRANSMISSION/MAILING										
I heraby certify that this or sufficient postage as first the date shown below: Signature					ed to: Commi	sslou	er for Patent			
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Typed or printed name	Jamie L	Toupal				П		Date	March 10, 2005	

Rea. No.

48,570

This collection of information is required by 37 CFR 1.5. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentially is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer. U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS. ADDRESS, SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No.:

ISPH-0752 (ISIS No RTS-0324US.C1)

Inventors:

C. Frank Bennett

Serial No.:

10/630,399

Filing Date:

July 30, 2003

Examiner:

Amy Hudson Bowman

Customer No.:

32,862

Group Art Unit:

1635

Title:

Antisense modulation of IL-1 Receptor-Associated

Kinase 4 expression

Certificate of Facstrulle Transmission I hereby certify that this paper is being facsimile transmitted to the Patent and Trademark Office to

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Janie I. Touvill
Commissioner for Patents
Alexandria, VA 22313

## Reply under 37 C.F.R. § 1.111

Dear Examiner Bowman:

This is a reply to the Office Action mailed February 10, 2005 setting a one (1) month period for response. Please enter the following amendments and remarks into the record.

The Amendments to the Claims are reflected in the listing of claims which begins on page 2.

Remarks begin on page 4.